

AMENDMENTS TO THE SPECIFICATION

Please amend the title as follows:

METHODS AND COMPOSITIONS OF ~~GENE~~ NUCLEIC ACID DELIVERY AGENTS FOR SYSTEMIC AND LOCAL THERAPY

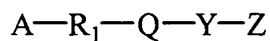
Please amend the paragraph beginning on line 19 of page 4 as follows:

The present invention has utility as a treatment for a variety of disease conditions or deficiencies. ~~These conditions and~~ The deficiencies illustratively include: ~~enzyme deficiency,~~ deficiencies in erythropoietin, catalase, endotoxic ~~shock/sepsis,~~ adenosine deaminase for treatment of severe combined immunodeficiency, lipid-binding protein (LBP), purine nucleotide phosphorylase, galactosidase, beta-glucuronidase, antioxidants for cancer, ~~therapy anemia,~~ superoxide dismutase, cancer, growth factors for use in wound healing, induction of red blood cell formation and the like, α -interferon, β -interferon, epidermal growth factor, granulocyte colony stimulating factor (G-CSF), alpha-IL1, gamma-interferon, phenylalanine ammonia lyase, transforming growth factor, arginase, erythropoietin, L-asparaginase, thrombopoietin, uricase, insulin-like growth factor-1, insulin, human growth hormone, monoclonal antibodies, tissue necrosis factor, cardiovascular disease, diabetes, tissue plasminogen activator, urokinase (native or chimeric), glucagon, α_1 -antitrypsin, insulintrophic hormone, clotting ~~disorders~~ factors, antithrombin-III, other proteases or protease inhibitors, clotting factor VIII, apolipoproteins (particularly B-48), circulating scavenger receptor, APO A1 which converts low-density lipoproteins to high-density lipoproteins, gastrointestinal and pancreatic deficiencies, obesity and feeding, pepsin (for esophageal reflux), Ob gene product, cholecystokinin (CCK), trypsin, chymotrypsin, bone diseases, elastase, carboxypeptidase, calcitonin, lactase (for lactose deficiency), PTH-like hormone, sucrase, intrinsic factor (pernicious anemia), myasthenia gravis

(acetylcholine receptors). These disease conditions that may be treated by the present invention include: Graves' disease (thyroid-stimulating hormone receptor), organ-specific autoimmune diseases (target of antibody in parentheses), thyroiditis (thyroid, peroxidase), insulin-resistant diabetes with acanthosis nigricans or with ataxia telangiectasia (insulin receptor), allergic rhinitis, asthma (β_2 -adrenergic receptors), juvenile insulin-dependent diabetes (insulin, GAD65), pernicious anemia (gastric parietal cells, vitamin B₁₂ binding site of intrinsic factor), Addison's disease (adrenal cells), idiopathic hypoparathyroidism (parathyroid cells), spontaneous infertility (sperm), premature ovarian failure (interstitial cells, corpus luteum cells), pemphigus (intercellular substance of skin and mucosa), bullous pemphigoid (basement membrane zone of skin and mucosa), primary biliary cirrhosis (mitochondria), autoimmune hemolytic anemia (erythrocytes), idiopathic thrombocytopenic purpura (platelet), idiopathic neutropenia (neutrophils), vitiligo (melanocytes), osteosclerosis and Meniere's disease (type II collagen), chronic active hepatitis (nuclei of hepatocytes), systemic autoimmune diseases (defect/organ affected in parentheses), Goodpasture's syndrome (basement membranes), rheumatoid arthritis (γ -globulin, EBV-related antigens, collagen types II and III), Sjogren's syndrome (γ -globulin, SS-A (Ro), SS-B (La), systemic lupus erythematosus (nuclei, double-stranded DNA, single-stranded DNA, Sm ribonucleoprotein, lymphocytes, erythrocytes, neurons, gamma-globulin), scleroderm (nuclei, Scl-70, SS-A (Ro), SS-B (La), centromere, polymyositis (nuclei, Jo-1, PL-7, histadyl-tRNA synthetase, threonyl-tRNA synthetase, PM-1, Mi-2), rheumatic fever (myocardium heart valves), and choroid plexus.

Please amend the paragraph beginning on line 15 of page 9 as follows:

An inventive conjugating agent has the general formula:



where ~~A—R₁~~ R₁ is a cholesterol derivative; a C₈-C₂₄ alkyl; C₈-C₂₄ heteroatom substituted alkyl wherein the heteroatom is O, N or S; where A is a hydrophilic moiety A that illustratively includes C₀-C₄ alkyl-hydroxy, -substituted amino, -quaternary amino, -sulfonate, -phosphonate, and -carboxylate; and targeting ligand; where the targeting ligand includes amino acids, hormones, antibodies, cell adhesion molecules, folate, polypeptides, vitamins, saccharides, ~~transferring transferrin~~, drugs, and neurotransmitters; where Q is sulfur, a secondary amine, or oxygen; where Y is a linker peptide having a negative, neutral, or positive charge; and where Z is a polyionic peptide. Specific examples of inventive cholesterol derivatives illustratively include cholestanol, coprostanol, cholic acid, glycocholic acid, ursoldeoxycholic acid, chenodeoxycholic acid, desoxycholic acid, glycochenodeoxycholic acid, taurocholic acid, and taurochenodeoxycholic acid. Specific examples of C₈-C₂₄ alkyls are 13-hydroxyl tridecanoic acid; 1,12 dodecane diol; and 1,12 dodecanediamine.